UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/589,688	04/16/2008	Mark I. Greene	UPN-5231	9908

23377 7590 07/21/2010

WOODCOCK WASHBURN LLP
CIRA CENTRE, 12TH FLOOR
2929 ARCH STREET
PHILADELPHIA, PA 19104-2891

EXAMINER	
LIU, SAMUEL W	
ART UNIT	**PAPER NUMBER**
1656	

MAIL DATE	DELIVERY MODE
07/21/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/589,688	GREENE ET AL.	
	Examiner	Art Unit	
	SAMUEL LIU	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *6/18/10 and 5/21/10*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-24 and 26* is/are pending in the application.

4a) Of the above claim(s) *24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-23* is/are rejected.

7)☒ Claim(s) *26* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 August 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/28/07, 1/23/09 , 5/12/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of claims

Claims 14-24 and 26 are pending.

The supplemental amendment filed 6/28/10 which amends claims 14, and cancels claims 1-13 and 25 has been entered.

Claim benefit

Applicant's claim for the benefit of a prior-filed application 60546224 filed 2/20/04 under 35 U.S.C. 119(e) is acknowledged. However, 60546224 does not have support for the elected invention (see below); and thus, this application does NOT have benefit of the filing date 2/20/04 thereof. The effective filing date of instant application is 2/18/05 the international filing date.

Election/election

The applicants' election (filed 5/21/10) of Group 8, claims 14-23 without traverse for examination is acknowledged. However, the election is incomplete because said lection does not respond to the "additional election" requirement under 35 USC 121 set forth at page 4 in the Office action mailed 5/12/010. Upon communication with applicants' representative Debora Plehn-Dujowich on 6/18/10, the additional election was made without traverse to prosecute (i) "antibodies" (from claim 15), (ii) "Her2" (from claim 16), and (iii) "biotinylated drug" (from claim 22) for examination. Affirmation of this election must be made by applicant in replying to this Office action.

New claim 26 which is directed to SEQ ID NO:8 which consists of (i) "Met Val Asp" linked to (ii) AHNP amino acid sequence "FCDGFYACYMDV" (SEQ ID NO:1) which is linked to a linker sequence of SEQ ID NO:11 which is linked to an amino acid sequence of the full-

length streptavidin amino acid sequence (SEQ ID NO:9) (from Glu38 to Ser163 in SEQ ID NO:9) which is linked to the C-terminal amino acid sequence of SEQ ID NO:8 "Asn Ser Ser Ser His His His His His His (SEQ ID NO:8) ". Thus, claim 26 is drawn to the elected invention and thus is examined.

Claim 24 (Group 9) is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Therefore, claims 14-23 and 26 are under examination.

IDS

The references cited in the information disclosure statement (IDS) filed 2/28/07, the IDS filed 1/23/09, and the IDS filed 5/12/10 have been considered by Examiner.

Objection to claims

Claims 15, 16 and 22 are objected to as containing non-elected subject matters "ligands for cell surface receptors, cell adhesion sequences, and antigens" (claim 15), "EGFR, VEGF, CEA, PSA, HER3, HER4, CD-20, TNF-, IL-1, TNFR, FAS, RANKL/TRANCE, OPG, CD40, CD28, CD3, CD4, IL-4 and IL- 13" (claim 16), and "a biotinylated toxin, a biotinylated nucleic acid molecule, a biotinylated radionuclide and a biotinylated detectable compound" (claim 22).

Claim 18 is objected to because "SEQ. ID NO:9" should be changed to "SEQ ID NO:9" for consistency.

Claim 21 is objected to because the "linker sequence "GGGGSRSNSSS" has been disclosed in "*Sequence Listing*" entered by PTO STIC as "SEQ ID NO:6"; and thus, SEQ ID NO:11" should be changed to "SEQ ID NO:6" thereof. Also, in claim 21, "a linker having a

linker sequence contains SEQ ID NO:11" should be changed to "a linker having a linker sequence that contains SEQ ID NO:11".

In claim 22, "the streptavidin" should be changed to "the streptavidin core sequence" for adequate antecedent basis.

In claim 23, "a protein of claim 14" should be changed to "the protein of claim 14".

Objection to specification

The disclosure is objected to because of the following informalities:

(1) At page 5, lines 5-6, for clarity, "construction of the AHNP fusion protein (ASA) and streptavidin (SA) expression vector" should be changed to "construction of the expression vector of AHNP fusion protein (ASA) and the expression vector of streptavidin (SA)".

(2) At page 5, line 13, "2-MT", "SDS" and "DTT" should be spelled out in full for the first instance of use. Similarly, see also page 5, line 20, "SDS-PAGE", and line 22, "ELISA"; page 9, line 1, "BOP"; and page 12, line 8, "RCA".

(3) At page 28, the amino acid sequence "GGGGSRSNSSS" should be assigned as SEQ ID NO:6 instead of "SEQ ID NO:11 since the entered (by PTO STIC") sequence has 100% sequence identity to said "SEQ ID NO:6".

(4) The specification is objected to as failing to provide proper antecedent basis for the claimed subject matters: "streptavidin wild type polypeptide containing amino acid residues 38 and 163 of SEQ ID NO:9" (claim 17); " streptavidin wild type polypeptide containing amino acid residues 41 and 16 of SEQ ID NO:9" (claim 18); "cell binding domain comprises SEQ ID

NO: 1" (claim 19); and "cell binding domain comprises SEQ ID NO: 10" (claim 20). See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction in these regard is required.

Objection to drawings

The drawing filed 8/17/06 is objected to under 37 CFR 1.83(a) because in Figure 4, "OD" lacks unit (at which wave length said OD value is reordered).

Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.

Claims 17-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 17-21 lack antecedent basis for "the cell binding domain" in claim 14 from which claims 17-21 depend.

Claim Rejections - 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 14, 15, 16, 19, 22 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Zhang et al. (WO02066980 A1) as is evidenced by Greene et al. (US 20030148932 A1).

Zhang et al. teach "AHNP-SA" fusion protein (recombinantly produced) comprising AHNP, a flexible linker $(Gly4Ser)_2$ and a core streptavidin (SA) sequence (p.13, lines 9-24); wherein AHNP is a constrained exocyclic peptide derived from the CDR3.H region of the anti-human p185 antibody (p.12, lines 26-30) and is capable of forming tetrameric AHNP mimetic complex (p.13, line 19), wherein AHNP has amino acid sequence "FCDGFYACYMDV" which reads on instant SEQ ID NO:1 as is evidenced by Greene et al. (Table 1, AHNP analogs "1" and "2"), and wherein the AHNP peptide is fused to N-terminus of the linker sequence that is fused to N-terminus of SA. The "AHNP-SA" structure meets the "binding peptidomimetic"

requirements set forth at page 6, lines 15-23 of instant specification. Thus, Zhang et al. teach claims 14, 15, 19 and 23.

The "AHNP-SA" protein binds Her2 (p.14, lines 1-2, and p.13, lines 7-8 and 31-34), which teaches claim 16.

Examiner remark: since "the cell binding domain" in claims 17-21 lacks antecedent basis in claim 14 (see above 112/2 rejection), for examination purpose, it is taken to be "binding peptidomimetic" retied in the amended claim 14.

Since binding of "SA" to biotinylated drug is considered to be an inherent property of the "AHNP-SA" fusion protein, claim 22 is rejected.

Claim Rejections - 35 USC §103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

[1] Claims 1, 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang et al. (WO02066980 A1) in view of Greene et al. (US 20030148932 A1) as applied to claim 14, and further in view of Atwell et al. (WO 9933965).

The teaching of claim 14 by the references Zhang and Greene et al. has been set forth above.

The above references do not expressly teach amino acid sequence of the core SA.

Atwell et al. teach the core amino acid sequence of SA which contains residue 22 (Glu 23) to residue 148 (Ser148) (see SEQ ID NO:3, Figure 10, and p.14, lines 16-18) equivalent to instant amino acids 38 to 163 of SEQ ID NO:9, as applied to claim 17.

The core amino acid sequence of SA which contains residue 26 (Ile26) to residue 148 (Ser148) (see SEQ ID NO:3, Figure 10, and p.14, lines 16-18) equivalent to instant amino acids 41 to 163 of SEQ ID NO:9, as applied to claim 18.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to construct the "AHNP-SA" fusion protein wherein "SA" portion comprises the core sequence of SA taught by Atwell et al. This is because the SA amino acid sequence and its cloning has been known in the art when the instant invention was made (p.29, line 1 to p.30, line 11), and because Atwell et al. have taught use of the core (the sequence necessary for SA binding activity) streptavidin in constructing the fusion protein comprising an antibody domain (P.14, lines 17-18, and Figures 4 and 11). Also, Atwell et al. have taught advantage of using the core SA which is shortened form of full-length SA with more soluble than the full-length and significantly enhanced binding activity for biotinylated proteins (Example 6, p.29, lines 12-19). Upon reading the Atwell reference, one of ordinary skill in the art would have cloned the SA core sequence and made fusion protein according to the Zhang et al., wherein the core SA sequence is fused with the AHNP peptide with reasonable expectation of success in the absence

of any unexpected results. Therefore, the reference's teaching renders the claims *prima facie* obvious.

[2] Claims 1 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang et al. (WO 02066980 A1) in view of Greene et al. (US 20030148932 A1).

The teaching of claim 14 by the references Zhang and Greene et al. has been set forth above.

Zhang et al, do not expressly teach the "AHNP" analog "**Y**CDGFYACYMDV" which reads on instant SEQ ID NO:10 and is an obvious variation of instant SEQ ID NO:1 "**F**CDGFYACYMDV".

In Table 1, Greene et al., however, teach the limited numbers of the AHNP analogs wherein the analog "**Y**CDGFYACYMDV" which show the highest binding ability to Her2 (see Table 1, analog "3"), as applied to claim 20.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to alternatively choose the AHNP analog such as "**Y**CDGFYACYMDV" with only difference in the first amino acid residue ("Y" substitute for "F"). This is because the AHNP is an anti-Her2 peptide mimetic derived from the structure of the CDR-H3 loop of the anti-Her2 rhum Ab 4D5 indicating its therapeutic usefulness (see [0167]). The binding ability to Her2 discussed above relates to anti-Hers antibody for treating advanced breast cancer (see [0163] and [0164]). Upon reading the Greene's teachings, one of ordinary skill in the art would have tried to substitute "**Y**CDGFYACYMDV" (SEQ ID NO:10) for "**F**CDGFYACYMDV" (SEQ ID NO:1) with reasonable expectation of success in the absence of any unexpected results.

Claim 26 is objected to as being dependent upon a rejected base claim 14, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Claims 14-23 are not allowed. Claim 26 is free from the prior art.

Any comments considered necessary by applicants must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Samuel Wei Liu, Ph.D. whose telephone number is (571) 272-0949. The Examiner can normally be reached daily except alternate Fridays from 8:30 A.M. to 5:30 P.M. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor Manjunath N. Rao can be reached at (571) 272-0939. The official fax number for Technology Center 1600 is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

/Samuel W. Liu/
Examiner, Art Unit 1656
/ANAND U DESAI/
Primary Examiner, Art Unit 1656
July 12, 2010